REMARKS

The Office Action has been carefully reviewed. No claim is allowed. Claims 18-23 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 20 and 21 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This new matter rejection is obviated by the amendment to claim 20.

Applicants believe that the amendment to claim 20 is supported by the following disclosure at page 9 of the specification (as amended December 19, 2001):

> The protein according to the present invention includes protein in general .... Variants ... can be obtained by replacing one or more amino acids in SEQ ID NO:2 ... variants, which are defective in or additionally contain one or more amino acids near to the N-terminal in SEQ ID NO:2 while retaining biological properties in the protein ... The present protein includes such variants as long as they induce the IFN- *y* production by immunocompetent cells.

SEQ ID NO:2 consists of 157 amino acid residues. As such, applicants believe that the upper limit of the number of amino acid residues replaced or deleted is 157. The language "one or more" must comprise "one or two" as the term "more" here is equivalent to "at least two". Therefore, there is support for the recitation of "one or two" in claim 20.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 20-23 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants believe that this rejection is obviated by the amendments to claims 20 and 22.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 18-23 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The examiner states that claims 18-23 are directed to a variant of IL-18, which encompasses variants having one or more amino acids in SEQ ID NO:2 replaced (claim 18, part (i), for example), one or more amino acids but not so many replaced (claim 20, part (i), for example), and variants not identical to SEQ ID

NO:2 (claim 22, for example), which read on functional equivalents of SEQ ID NO:2 as there is no clear limitation as to how many amino acids can be replaced in SEQ ID NO:2. The examiner considers the claims to encompass significant structural dissimilarity as compared to the exemplified IL-18 and the variants, including functional equivalents without any sequence similarity to the disclosed SEQ ID NO:2. The examiner further indicates that the specification however discloses one IL-18 amino acid sequence with particularity, the murine IL-18 with SEQ ID NO:2, and no particular variant of the IL-18 with amino acid addition, deletion, substitution, or any other type of "functional equivalents" meeting the limitations of these claims were ever identified or particularly described. This rejection is respectfully traversed.

Applicants would like to point out that an isolated variant of IL-18 is limited by its amino acid sequences (please see parts (i) to (iii) of claim 20), its function of inducing IFN-γ production, its purity (i.e., exhibits a single protein band when electrophoresed on SDS-PAGE), and its molecular weight of 19,000 + 5,000 daltons. Applicants believe that one of skill in the art could have easily obtained such a variant as defined in claims 20 or 22, once the amino acid sequence of SEQ ID NO:2

was given, based on the recombinant DNA technology known to the public at the time of the present application was file.

Attached hereto is J.D. Watson et al. "Recombinant DNA", second edition, SCIENTIFIC AMERICAN BOOKS, 1992, pp. 191-211, 453-470 in support of enablement. Please see page 193, left column; page 201, right and left columns; the paragraph bridging pages 204 and 206 of the attached publication. In particular, page 466, right column, teaches as follows:

> This experiment points out the power of recombinant DNA as a tool for the engineering of natural products. Changing the properties of a protein was all but impossible prior to the development of recombinant DNA techniques. Now it is not only possible, but easy. It is a routine exercise for protein engineers to generate hundreds of variants of a natural protein for testing. These changes can be educated guesses based on detailed knowledge of the structure of a protein; alternatively, changes can easily be made on a purely random basis. And, as we will see in the next section, a combination of structural information with random mutagenesis and a powerful selection for improved protein function can have dramatic results. (emphasis added)

Also attached hereto are copies of US Patent Nos. 5,830,715 (please see claim 1) and 5,922,578 (please see claim 1), which show that obtaining various variants was routine (i.e., merely routine experimentation) for one of skill in the art at the time the present application was filed.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. and define patentable subject matter warranting its allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /ACY/
Allen C. Yun
Registration No. 37,971

ACY:pp
624 Ninth Street, N.W.
Washington, D.C. 20001
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\S\SUMA\Okamura2E\pto\2007-11-08amendment.doc